Applicant: Bonner-Weir et al. Attorney's Doc. No.: 10276-029001 / JDP-044

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## Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

## Listing of Claims:

Claims 1-28 (Canceled)

Claim 29. (Currently Amended) A method of obtaining pancreatic islet cells, the method comprising:

obtaining a population of dedifferentiated pancreatic cells made by (a) providing differentiated pancreatic duct or exocrine cells substantially free of islet cells, and (b)

allowing said <u>differentiated</u> duct or exocrine cells to proliferate to form a population of dedifferentiated pancreatic cells, said proliferation being characterized by (i) lack of insulin expression and (ii) expression of one or more of IPF-1, PDX-1, STF-1, IDX-1 and Prof 1 protein;

adding a component of extracellular matrix (ECM) to the population of dedifferentiated pancreatic cells; and

growing the cells in the presence of the component of ECM for a time sufficient for the dedifferentiated cells to express insulin, thereby obtaining pancreatic islet cells.

Claim 30. (Previously Added) The method of claim 29, wherein the population of dedifferentiated pancreatic cells has been cultured until at least about 70% confluency before adding a component of the extracellular matrix.

Claim 31. (Canceled)

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Claim 32. (Currently Amended) The method of claim 29 31, wherein the dedifferentiated pancreatic cells express cytokeratin.

- Claim 33. (Previously Added) The method of claim 29, wherein the component of extracellular matrix is laminin.
- Claim 34. (Previously Added) The method of claim 29, wherein the component of extracellular matrix is a basement membrane derived substance.
- Claim 35. (Previously Added) The method of claim 34, wherein the basement membrane is laid down by an Engelbreth-Holm-Swarm tumor cell.
- Claim 36. (Previously Added) The method of claim 29, wherein the component of extracellular matrix is added by overlaying the population of dedifferentiated cells.
- Claim 37. (Previously Added) The method of claim 29, wherein at least a portion of the cultured cells form cultivated islet buds.
- Claim 38. (Previously Added) The method of claim 37, wherein the cultivated islet buds comprise hormone positive islet cells.
- Claim 39. (Previously Added) The method of claim 37, wherein the cultivated islet cells express increased levels of insulin expression as compared to the dedifferentiated cells.
- Claim 40. (Previously Added) The method of claim 29, wherein the pancreatic islet cells have the ability to secrete insulin in response to glucose.

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Claim 41. (Currently Amended) A method of obtaining pancreatic islet cells, the method comprising:

- (a) obtaining a population of dedifferentiated pancreatic cells made by the process of:
- (i) obtaining a population of adult or differentiated pancreatic cells substantially free of islet cells, and
- (b) (ii) allowing the adult or differentiated pancreatic cells to proliferate to form a population of dedifferentiated pancreatic cells, said proliferation being characterized by (i) lack of insulin expression and (ii) expression of one or more of IPF 1, PDX 1, STF 1, IDX 1 and Pref 1 protein;
- (c) (b)-adding a component of extracellular matrix (ECM) to the population of dedifferentiated pancreatic cells; and
- (d) (e) growing the cells in the presence of the component of ECM for a time sufficient for the dedifferentiated cells to express insulin, thereby obtaining pancreatic islet cells.
- Claim 42. (Previously Added) The method of claim 41, wherein the population of adult or differentiated pancreatic cells substantially free of islet cells is obtained from cells remaining after islet isolation from a pancreatic tissue.
- Claim 43. (Previously Added) The method of claim 41, wherein the population of adult or differentiated pancreatic cells substantially free of islet cells is selected based on the ability to adhere to a container.

## Claim 44. (Canceled)

Claim 45. (Currently Amended) The method of claim 41 [[44]], wherein the dedifferentiated pancreatic cells express cytokeratin.

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Claim 46. (Previously Added) The method of claim 41, wherein the component of extracellular matrix is laminin.

Claim 47. (Previously Added) The method of claim 41, wherein the component of extracellular matrix is added by overlaying the population of dedifferentiated cells.

Claim 48. (Previously Added) The method of claim 41, wherein at least a portion of the cultured cells form cultivated islet buds.

Claim 49. (Previously Added) The method of claim 48, wherein the cultivated islet buds comprises hormone positive islet cells.

Claim 50. (Canceled)

Claim 51. (Previously Added) The method of claim 41, wherein the pancreatic islet cells have the ability to secrete insulin in response to glucose

Claim 52. (Previously Added) The method of claim 41, wherein an agent that promotes expansion is added to the adult or differentiated pancreatic cells.

Claim 53. (Previously Added) The method of claim 52, wherein the agent is a growth factor or a combination of growth factors.

Claim 54. (Previously Added) The method of claim 53, wherein the growth factor is selected from the group consisting of: keratinocyte growth factor, epidermal growth factor, transforming growth factor- $\alpha$ , hepatocyte growth factor, and combinations thereof.

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Claim 55. (Previously Added) The method of claim 54, wherein the growth factor is keratinocyte growth factor.

Claim 56. (Previously Added) The method of claim 41, wherein the adult or differentiated pancreatic cells are placed on a substrate in a glucose-containing media.

Claim 57. (Previously Added) The method of claim 41, wherein the population of adult or differentiated pancreatic cells is cultured until at least about 70% confluency before adding the component of extracellular matrix.

Claims 58-60. (Canceled)

Claim 61. (Currently Amended) The method of claim 14, 29 or 41, wherein the component of extracellular matrix is collagen.

Claim 62. (Currently Amended) The method of claim 14, 29 or 41, wherein the component of extracellular matrix is entactin.

Claim 63. (Currently Amended) The method of claim 14, 29 or 41, wherein the component of extracellular matrix is heparin sulfate proteoglycan.

Claim 64. (Currently Amended) The method of claim 14, 29 or 41, wherein the component of extracellular matrix is nidogen.

Claims 65-67. (Canceled)

Claim 68. (Previously Presented) The method of claim 29, wherein the proliferation is characterized by expression of IPF-1.

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Claim 69. (Previously Presented) The method of claim 29, wherein the proliferation is characterized by expression of PDX-1.

- Claim 70. (Previously Presented) The method of claim 29, wherein the proliferation is characterized by expression of Pref-1.
- Claim 71. (Previously Presented) The method of claim 41, wherein the proliferation is characterized by expression of IPF-1.
- Claim 72. (Previously Presented) The method of claim 41, wherein the proliferation is characterized by expression of PDX-1.
- Claim 73. (Previously Presented) The method of claim 41, wherein the proliferation is characterized by expression of Pref-1.